(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number
WO 2004/042015 A3

(51) International Patent Classification[7]: A61K 48/00, C12N 15/861, 15/863

(21) International Application Number: PCT/US2003/034599

(22) International Filing Date: 31 October 2003 (31.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/423,244 1 November 2002 (01.11.2002) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/423,244 (CON)
Filed on 1 November 2002 (01.11.2002)

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
12 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/042015 A3

(54) Title: METHODS AND VECTORS FOR CONTROLLING GENE EXPRESSION

(57) Abstract: Viral vectors that include a nucleic acid encoding a therapeutic polypeptide operably linked to a heterologous destabilizing element are described.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/34599

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 48/00; C12N 15/861, 15/863
US CL : 435/320.1, 455, 456; 424/93.2; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/320.1, 455, 456; 424/93.2; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	AHMED et al. A conditionally replicating adenovirus targeted to tumor cells through activated RAS/P-MAPK-selective mRNA stabilization. Nature Biotechnology. July 2003, Vol. 21, No. 7, pages 771-777, see entire reference.	1, 2, 6-8, 12-15, 17-19, 21
X	US 5,925,564 A (SCHWARTZ et al.) 20 July 1999 (20.07.1999), see entire reference, especially column 2, line 56, to column 3, line 7; column 5, line 65 to column 6, line 26; column 7, line 66, to column 8, line 29; column 9, lines 1-20; column 10, lines 11-34; column 12, lines 2-8; column 14, lines 36-53; column 30, lines 32-41; columns 32-37.	1, 22
X	WO 98/56936 A1 (MAX PLANCK GESELLSCHAFT ZUR FOEDERUNG DER WISSENSCHAFTEN) 17 December 1998 (17.12.1998), see entire document, especially pages 4-7, 11-12, 15-18, and claims 1, 10, 11, 13, 15, 16, 19, 40, 41, 43, 45.	1, 2, 9, 10, 22
X	BOAST et al. Characterization of physiologically regulated vectors for the treatment of ischemic disease. Human Gene Therapy. 01 September 1999, Vol. 10, No. 13, pages 2197-2208, especially page 2200, Table 2; page 2203, and page 2204, Figure 4.	1, 2, 9, 10, 22

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search
12 March 2004 (12.03.2004)

Date of mailing of the international search report
27 MAY 2004

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Form PCT/ISA/210 (second sheet) (July 1998)

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SHENG et al. Transforming growth factor-beta1 enhances Ha-ras-induced expression of cyclooxygenase-2 in intestinal epithelial cells via stabilization of mRNA. Journal of Biological Chemistry. 03 March 2000, Vol. 275, No. 9, pages 6628-6635.	1, 7-9
A	DIBBENS et al. Hypoxic regulation of vascular endothelial growth factor mRNA stability requires the cooperation of multiple RNA elements. Molecular Biology of the Cell. April 1999, Vol. 10, pages 907-919.	1, 2, 9-10, 12-22
A	NABORS et al. HuR, a RNA stability factor, is expressed in malignant brain tumors and binds to adenine- and uridine-rich elements within the 3' untranslated regions of cytokine and angiogenic factor mRNAs. Cnacer Research. 01 March 2001, Vol. 61, No. 5, pages 2154-2161.	1, 2, 4-22
A	SHIBATA et al. Development of a hypoxia-responsive vector for tumor-specific gene therapy. Gene Therapy. March 2000, Vol. 7, No. 6, pages 493-498.	1-2, 9, 10, 12-22

INTERNATIONAL SEARCH REPORT

PCT/US03/34599

Continuation of B. FIELDS SEARCHED Item 3:

USPT, PGPB, DWPI, MEDLINE, EMBASE, BIOSIS, CAPLUS, SCISEARCH

search terms: mRNA, UTR, untranslated region, destabil?, stabil?, gene therap?, tumor, cancer, Ahmed A?, Vile R?, uPAR, urokinase plasminogen activator receptor, cox2, cyclooxygenase 2, RAS, VEGF, TNF alpha, tumor necrosis factor alpha,